

Roche

EGFR tyrosine kinase domain with erlotinib.

Soloway, MD, of Memorial Regional Hospital in Hollywood, FL.

McKiernan agrees. A clinical trial “is a no-brainer,” he says. ■

EMA to Publish Clinical Trial Reports

In a move toward full transparency, European regulators will soon publish clinical trial reports on all drugs approved for marketing in the European Union (EU).

The policy, which was approved in principle on June 12 by the European Medicines Agency’s (EMA) management board, is expected to be formally adopted at the board’s October 2 meeting. The move will allow researchers to download clinical trial reports from the organization’s website, enabling them to analyze, share, and compare trial data once the decision-making process for the medicine in question has been completed.

“We began giving access to clinical study reports in 2010, and we’ve released well over 2 million pages of reports since then,” says Martin Harvey, EMA spokesperson. “The big difference now is that instead of waiting for researchers to formally request access to documents, we will proactively publish them on our website.”

For now, reports published on the website will not include anonymous patient-level data, which contain complete information on each participant in a trial (as opposed to aggregate or summary data). Researchers can still obtain such data but must formally request it until the EMA works out privacy-protection issues and finalizes guidelines in a second phase of the policy.

The EMA policy has provoked debate since it was first introduced in May 2013. Although researchers and patient

groups have pushed for full transparency—provided that the identities of patients are protected—pharmaceutical companies have objected to sharing data with competitors. However, EMA regulators have contended that open access to data ultimately benefits all sides.

“Contrary to industry fears, we argue that access to full—though appropriately de-identified—data sets from clinical trials will benefit the research-based biopharmaceutical industry,” wrote EMA executive director Guido Rasi, MD, and colleagues last year (*N Engl J Med* 2013;369:1577-9). “We predict that it will help to increase the efficiency of drug development, improve cost-effectiveness, improve comparative-effectiveness analysis, and reduce duplication of effort among trial sponsors.”

To address industry concerns, the policy allows companies to request redaction of information deemed commercially confidential, such as details of manufacturing processes or exploratory endpoints that a company may have been pursuing at the time of submission but have not yet been approved, says Harvey. The final rule will contain full details on what types of requests the EMA will consider.

Although some critics of the policy worry that companies will have too much control over withholding data, Harvey notes that most of the data in clinical study reports does not qualify as commercially confidential.

“Our redaction principles will lay out the only areas where we are prepared to consider exceptions, and the final decision is ours,” he says. In addition, the extent and type of information redacted will be visible on the EMA website.

The EMA is the first major drug regulatory agency to propose publishing participant-level clinical trial reports on specific approved drugs. The FDA has proposed making trial data available without linking it to specific products or applications by, for example, releasing certain data from a random sample or pooling data within one product class.

“The FDA’s concept is to develop a framework to make publicly available non-summary safety and effectiveness data that has been de-identified and masked,” says Stephen King, spokesperson for the FDA’s Center for Drug Evaluation and Research. “The data

made available under this framework could be used, for example, to help further understanding of potential biomarkers, endpoints, and drug-development tools to improve public health and stimulate innovation in medical product development.” ■

CTCs Could Guide Cancer Therapy

Researchers have shown that rare tumor cells circulating in a patient’s blood can be cultured and genetically analyzed. The approach, described in *Science* in July, demonstrates that it may be possible to use a simple blood draw to track a cancer as it evolves and adjust treatment accordingly (*Science* 2014;345:216-20).

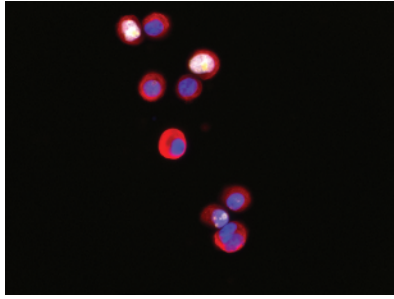
Scientists isolated circulating tumor cells (CTC)—cancer cells shed by solid tumors—from the blood of 36 patients with metastatic estrogen receptor-positive breast cancer. CTC cell lines from six patients were successfully grown in the lab and screened for mutations in 1,000 cancer-associated genes, revealing new mutations that were not present in the primary tumors.

Tumors have learned to adapt to effective treatments by changing their genetic make-up, says co-senior author Daniel Haber, MD, PhD, director of the Massachusetts General Hospital (MGH) Cancer Center in Boston. Indeed, CTCs from three patients treated extensively with estrogen-blocking aromatase inhibitors tested positive for an uncommon estrogen receptor mutation. Another patient’s cancer developed new mutations in both *PI3K* and *FGFR*.

Subsequent testing found various targeted drugs could inhibit cancer growth in patient-derived cell lines and in mice with tumors developed from each patient’s CTCs.

The existence of CTCs has been known for nearly 150 years. They are exceedingly rare, with a single cancer cell drifting among a billion healthy blood cells. To date, they have been useful only in predicting a patient’s prognosis.

In the study, CTCs were captured using the MGH-developed CTC-iChip, which Johnson & Johnson (J&J) will develop for commercial use. The device can capture CTCs in nearly 80% of patients with metastatic cancer, whereas



Min Yu and Maria C. Donaldson

CTCs isolated and cultured from the peripheral blood of a patient with breast cancer. Cytokeratin is shown in red; Ki67 in yellow; CD45 in green; and nuclei in blue.

CellSearch (Janssen Diagnostics, a J&J subsidiary)—the only FDA-approved test for isolating CTCs—is successful only about half the time, says Haber. In addition, the new device harvests living tumor cells, as opposed to CellSearch, which fixes CTCs for counting.

The microchip works by first removing small blood components. The remaining white blood cells and CTCs are aligned single file using a microfluidic process. White blood cells are magnetically tagged and deflected, leaving behind untouched CTCs. Previous research shows the CTC-iChip can capture CTCs from the blood of patients with advanced cancers of the prostate, lung, pancreas, and colon (*Sci Transl Med* 2013;5:179ra47).

It takes only 30 minutes to process a blood sample, but the CTC culturing process can take 1 to 3 months. Even then, not all CTCs can be grown in the lab. “The technology isn’t perfect yet,” says Haber, whose team is working to improve the device’s capture rate and speed up culturing. Haber expects it will be 1 to 2 years before the device is moved into clinical testing.

Jeffrey Smerage, MD, PhD, who conducts research on CTCs at the University of Michigan Comprehensive Cancer Center in Ann Arbor, agrees the technology is not ready for routine clinical use.

Smerage, who was not involved in the study, says researchers must still determine how methods used to grow CTCs influence their gene expression and whether CTCs and metastatic tumors are biologically the same. Even so, the findings make Smerage “very optimistic” about the possibility of using CTCs to guide therapy. ■

For more news on cancer research, visit *Cancer Discovery* online at <http://CDnews.aacrjournals.org>.

French Collaboration to Advance Data Analysis

Genetic analysis offers unprecedented power to diagnose tumors and target therapies, but it also brings the challenge of managing many gigabytes of data. Now, a French collaboration has formed to develop advanced scientific software that will help make sense of all this information.

The Interpretation of Clinical Exome, or ICE, project includes French cancer center Gustave Roussy; the French National Health and Medical Research Institute, known as Inserm, which is providing nearly \$3 million; and two companies: the genomics services firm IntegraGen and an engineering and technology consulting firm, Sogeti High Tech. The four collaborators bring expertise in genomic sequencing, data management, software development, and clinical practice.

Bernard Courtieu, chairman and CEO of IntegraGen, says sequencing a single patient takes 20 gigabytes of data, and matching that with the dozens of targeted drugs expected to be approved in the next few years will be a major choke point in care. The main goal, he says, will be to match the patient’s genomic profile with available drugs, something that will soon be too complex for doctors to do on their own.

The ICE Program also intends to provide what a U.S. oncologist describes as “genomic profiling for dummies,” so that doctors who have a limited amount of time to spend with a patient will be able to derive and share meaningful information about that person’s profile.

The collaborators expect to complete an early version of the software in 2016, at which point the market for new genomic interpretation tools will be valued at around \$5.4 billion, Courtieu estimates.

Other companies and collaborators are trying to solve the same data problems. What will set ICE’s technology apart, Courtieu says, will be the focus on the doctor and patient, rather than maximizing the technology for its own sake. Doctors, he says, are “looking for meaningful actionable pieces of information.” ■

NOTED

- **The FDA granted traditional approval to idelalisib (Zydelig; Gilead) for use with rituximab (Rituxan; Genentech) for the treatment of relapsed chronic lymphocytic leukemia.** The agency also granted accelerated approval to the drug for the treatment of relapsed follicular B-cell non-Hodgkin lymphoma and relapsed small lymphocytic lymphoma.
- **Roche announced that a phase III study of the MEK inhibitor cobimetinib met its primary endpoint.** Used in combination with Roche’s BRAF inhibitor vemurafenib (Zelboraf), cobimetinib helped patients with previously untreated BRAF V600 mutation-positive advanced melanoma live significantly longer without their disease worsening compared with vemurafenib alone.
- **GlaxoSmithKline halted a phase III trial of its MEK inhibitor trametinib (Mekinist) in combination with its BRAF inhibitor dabrafenib (Tafinlar) based on an interim analysis showing an overall survival benefit.** The trial was comparing the combination to vemurafenib in patients with BRAF V600E or V600K mutation-positive advanced melanoma.
- **New York’s Cold Spring Harbor Laboratory received a \$50 million gift from the Jim and Marilyn Simons Foundation** to establish a center focused on using quantitative biology to interpret genomic research data from a variety of diseases.
- **Los Angeles, CA–based Puma Biotechnology announced that women with early-stage HER2-positive breast cancer who took neratinib (PB272) for adjuvant treatment of their disease as part of a phase III clinical trial experienced 33% improvement in disease-free survival** compared with those who took a placebo. Based on the study’s findings, Puma plans to file for FDA approval of neratinib in 2015.
- **The American Thoracic Society, American College of Chest Physicians, and other organizations in the Forum of International Respiratory Societies issued a position statement taking a dim view of electronic cigarettes.** “As a precaution,” the statement reads, “electronic nicotine-delivery devices should be restricted or banned until more information about their safety is available. If they are allowed, they should be closely regulated as medicines or tobacco products.”